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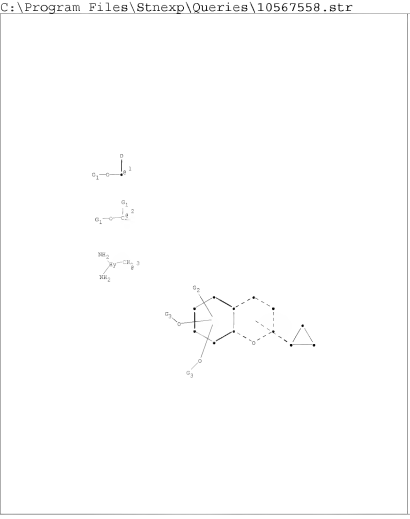

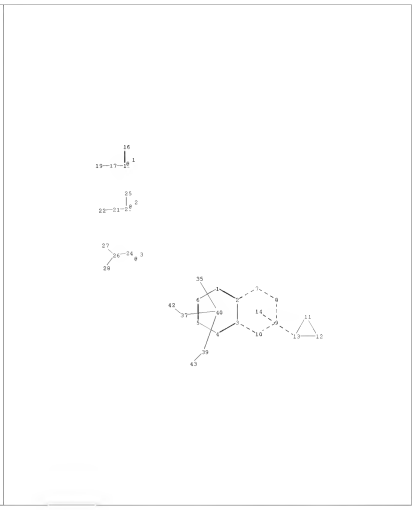

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chain nodes :
    15  16  17  19  20  21  22  24  25  26  27  28  35  37  39  42  43
ring nodes :
    1  2  3  4  5  6  7  8  9  10  11  12  13
chain bonds :
    15-16  15-17  17-19  20-21  20-25  21-22  24-26  26-27  26-28  37-42  39-43
ring bonds :
    1-2  1-6  2-3  2-7  3-4  3-10  4-5  5-6  7-8  8-9  9-10  11-12  11-13  12-13
exact/norm bonds :
    2-7  3-10  7-8  8-9  9-10  15-16  15-17  17-19  20-21  20-25  21-22  24-26  26-27  26-28  37-42
    39-43
exact bonds :
    11-12  11-13  12-13
normalized bonds :
    1-2  1-6  2-3  3-4  4-5  5-6
isolated ring systems :
    containing 1 : 11 :


G1:H,CH3,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu

G2:[*1],[*2],[*3]

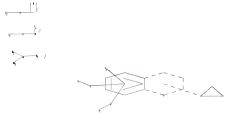
G3:H,CH3,Et

Match level :
    1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom  11:Atom
    12:Atom  13:Atom  14:Atom  15:CLASS  16:CLASS  17:CLASS  19:CLASS  20:CLASS  21:CLASS  22:CLASS
    24:CLASS  25:CLASS  26:Atom  27:CLASS  28:CLASS  35:CLASS  36:Atom  37:CLASS  38:Atom  39:CLASS
    40:Atom  42:CLASS  43:CLASS
Generic attributes :
    26:
    Saturation              : Unsaturated
    Number of Carbon Atoms : less than 7
    Number of Hetero Atoms : 2 or more
```

Type of Ring System : Monocyclic

Element Count :
Node 26: Limited
C,C4
N,N2
O,O0
S,S0

=>
Uploading C:\Program Files\Stnexp\Queries\10567558.str



chain nodes :
15 16 17 19 20 21 22 24 25 26 27 28 35 37 39 42 43
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13
chain bonds :
15-16 15-17 17-19 20-21 20-25 21-22 24-26 26-27 26-28 37-42 39-43
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10 11-12 11-13 12-13
exact/norm bonds :
2-7 3-10 7-8 8-9 9-10 15-16 15-17 17-19 20-21 20-25 21-22 24-26 26-27
26-28 37-42 39-43
exact bonds :

```
11-12  11-13  12-13
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6
isolated ring systems :
containing 1 : 11 :


G1:H,CH3,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu

G2:[*1],[*2],[*3]

G3:H,CH3,Et

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:CLASS  16:CLASS  17:CLASS  19:CLASS
20:CLASS  21:CLASS  22:CLASS  24:CLASS  25:CLASS  26:Atom  27:CLASS  28:CLASS
35:CLASS  36:Atom  37:CLASS  38:Atom  39:CLASS  40:Atom  42:CLASS  43:CLASS
Generic attributes :
26:
Saturation              : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : 2 or more
Type of Ring System    : Monocyclic

Element Count :
Node 26: Limited
    C,C4
    N,N2
    O,O0
    S,S0




L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1 sss sam
SAMPLE SEARCH INITIATED 16:36:58 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      851 TO ITERATE

100.0% PROCESSED      851 ITERATIONS                              1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
```

```
PROJECTED ITERATIONS:        15270 TO    18770
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

=> => s l1 sss ful
FULL SEARCH INITIATED 16:37:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    17119 TO ITERATE

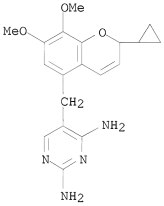
100.0% PROCESSED    17119 ITERATIONS                                 17 ANSWERS
SEARCH TIME: 00.00.01

L3           17 SEA SSS FUL L1

=> => s l3
L4           47 L3

=> d l4 1-47 bib,ab,hitstr
```

L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:1267885 CAPLUS
DN 151:398747
TI In vitro bactericidal activity of iclaprim in human plasma
AU Laue, Heike; Valensise, Tiziana; Seguin, Aurelie; Lociuro, Sergio; Islam, Khalid; Hawser, Stephen
CS Givaudan Schweiz AG, Duebendorf, Switz.
SO Antimicrobial Agents and Chemotherapy (2009), 53(10), 4542-4544
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB This study evaluated the effect of human plasma on the in vitro bactericidal activity of the novel diaminopyrimidine iclaprim against methicillin-susceptible and -resistant Staphylococcus aureus strains. MICs and minimal bactericidal concns. (MBCs) of iclaprim, with .apprx.93% protein binding, were similar in the absence and in the presence of 50% human plasma; MICs and MBCs ranged from 0.06 to 0.125 μg/mL. Furthermore, the activity of iclaprim was not affected by plasma, with ≥99.9% reduction in CFU after 5.0 to 7.6 h.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic activity of iclaprim in human plasma against Staphylococcus aureus)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)

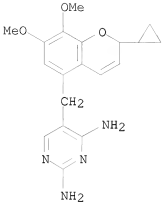


RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:1262760 CAPLUS
DN 151:433924
TI Aqueous pharmaceutical formulation comprising 5-[(2RS)-2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-ylmethyl]-pyrimidine-2,4-diamine methanesulfonic salt for bolus injection or i.v. infusion
IN Gillessen, Dieter; Jaeger, Juergen
PA Arpida A.-G., Switz.
SO PCT Int. Appl., 35pp.; Chemical Indexing Equivalent to 151:433860 (US)
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2009124586	A1	20091015	WO 2008-EP54232	20080408
	W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	US 20090253722	A1	20091008	US 2008-99284	20080408
PRAI	US 2008-99284	T0	20080408		

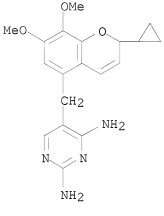
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention concerns a stable aqueous pharmaceutical composition comprising 5-[(2RS)-2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-ylmethyl]-pyrimidine-2,4-diamine in form of the water soluble methanesulfonic acid salt, a physiol. sodium chloride solution, ethanol and Povidone 12 PF, the liquid having a pH of over and above 4.8, but not higher than 5.2, and wherein the oxygen amount is controlled to be 0.8 ppm or less; which can be sterilized by filtration and/or by heated treatment, stored for longer time periods and which can be use for bolus injection or diluted for i.v. infusion.
IT 192314-93-5D, Iclaprim, addition salt 474793-41-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aqueous pharmaceutical formulation comprising 5-[(2RS)-2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-ylmethyl]-pyrimidine-2,4-diamine methanesulfonic salt for bolus injection or i.v. infusion)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



RN 474793-41-4 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 192314-93-5
CMF C19 H22 N4 O3



CM 2

CRN 75-75-2
CMF C H4 O3 S

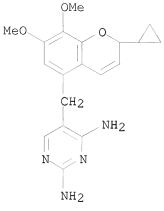
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:1228436 CAPLUS
DN 151:433860
TI Aqueous pharmaceutical formulation comprising 5-[(2RS)-2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-ylmethyl]-pyrimidine-2,4-diamine methanesulfonic salt for bolus injection or i.v. infusion
IN Gillessen, Dieter; Jaeger, Juergen
PA Arpida AG, Switz.
SO U.S. Pat. Appl. Publ., 10pp.; Chemical Indexing Equivalent to 151:433924 (WO)
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 20090253722	A1	20091008	US 2008-99284	20080408
WO 2009124586	A1	20091015	WO 2008-EP54232	20080408

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

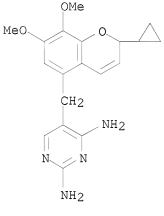
PRAI US 2008-99284 T0 20080408
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention concerns a stable aqueous pharmaceutical composition comprising 5-[(2RS)-2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-ylmethyl]-pyrimidine-2,4-diamine in form of the water soluble methanesulfonic acid salt, a physiol. sodium chloride solution, ethanol and Povidone 12 PF, the liquid having a pH of over and above 4.8, but not higher than 5.2, and wherein the oxygen amount is controlled to be 0.8 ppm or less; which can be sterilized by filtration and/or by heated treatment, stored for longer time periods and which can be use for bolus injection or diluted for i.v. infusion.
IT 192314-93-5D, Iclaprim, addition salt 474793-41-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aqueous pharmaceutical formulation comprising 5-[(2RS)-2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-ylmethyl]-pyrimidine-2,4-diamine methanesulfonic salt for bolus injection or i.v. infusion)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



RN 474793-41-4 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 192314-93-5
CMF C19 H22 N4 O3



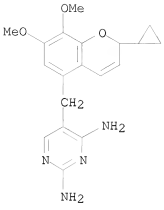
CM 2

CRN 75-75-2
CMF C H4 O3 S

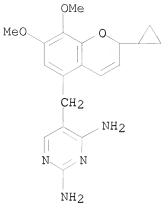
L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:1194632 CAPLUS
DN 151:418165
TI Gene expression profiling in the pulmonary artery in the selection of therapies for vascular-related diseases
IN Mann, David Marshall
PA Vascular Biosciences, Inc., USA
SO PCT Int. Appl., 115pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2009121031	A1	20091001	WO 2009-US38685	20090327
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2008-40065P	P	20080327		

AB Methods of selecting treatment regimens for vascular-related diseases and disorders using gene expression profiles in affected blood vessels are described. Addnl., methods are disclosed involving diagnostic techniques to focus treatment regimens. Finally, methods of treating vascular-related disorder involving targeting microRNAs are also disclosed. Therapies suitable for treatment at different stages of the disease are identified.
IT 192314-93-5, Iclaprim
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in treatment of vascular disease; gene expression profiling in pulmonary artery in selection of therapies for vascular-related diseases)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)

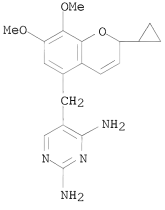

OMe
MeO
O
CH2
NH2
N
N
NH2

L4 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:1139997 CAPLUS
DN 151:332024
TI Efficacy of iclaprim against wild-type and thymidine kinase-deficient methicillin-resistant Staphylococcus aureus isolates in an in vitro fibrin clot model
AU Entenza, Jose M.; Haldimann, Andreas; Giddey, Marlyse; Lociuro, Sergio; Hawser, Stephen; Moreillon, Philippe
CS Department of Fundamental Microbiology, University of Lausanne, Lausanne, 1015, Switz.
SO Antimicrobial Agents and Chemotherapy (2009), 53(9), 3635-3641
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Iclaprim is a novel diaminopyrimidine antibiotic that is active against methicillin-resistant Staphylococcus aureus (MRSA). However, it is known that the activity of diaminopyrimidines against S. aureus is antagonized by thymidine through uptake and conversion to thymidylate by thymidine kinase. Unlike with humans, for whom thymidine levels are low, thymidine levels in rodents are high, thus precluding the accurate evaluation of iclaprim efficacy in animal models. We have studied the bactericidal activity of iclaprim against an isogenic pair of MRSA isolates, the wild-type parent AW6 and its thymidine kinase-deficient mutant AH1252, in an in vitro fibrin clot model. Clots, which were aimed at mimicking vegetation structure, were made from human or rat plasma containing either the parent AW6 or the mutant AH1252, and they were exposed to homologous serum supplemented with iclaprim (3.5 μg/mL), trimethoprim-sulfamethoxazole (TMP-SMX; 8/40 μg/mL), vancomycin (40 μg/mL), or saline, each of which was added one time for 48 h. In rat clots, iclaprim and TMP-SMX were bacteriostatic against the parent, AW6. In contrast, they were bactericidal (≥3 log10 CFU/clot killing of the original inoculum) against the mutant AH1252. Vancomycin was the most active drug against AW6 ($P < 0.05$), but it showed an activity similar those of iclaprim and TMP-SMX against AH1252. In human clots, iclaprim was bactericidal against both AW6 and AH1252 strains and was as effective as TMP-SMX and vancomycin ($P > 0.05$). Future studies of animals using simulated human kinetics of iclaprim and thymidine kinase-deficient MRSA, which eliminate the thymidine-induced confounding effect, are warranted to support the use of iclaprim in the treatment of severe MRSA infections in humans.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic activity of iclaprim against wild-type and thymidine kinase-deficient methicillin-resistant Staphylococcus aureus)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



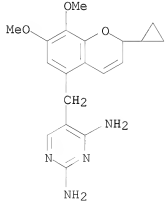
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:902223 CAPLUS
DN 151:142941
TI Antimicrobial development in the era of emerging resistance
AU Sorlozano, Antonio; Carrasco, Cristina; Cabeza, Jose; Villegas, Enrique; Gutierrez, Jose
CS Department of Microbiology, School of Medicine, University of Granada, Spain
SO Mini-Reviews in Medicinal Chemistry (2009), 9(8), 938-955
CODEN: MMCIAE; ISSN: 1389-5575
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
AB A review. Antibiotics currently under study by the Food and Drugs Administration include: faropenem (for treatment of sinusitis, bronchitis, and community-acquired pneumonia), dalbavancin (for catheter infections), telavancin (for treatment of nosocomial pneumonia), oritavancin (for bacteremia), ceftobiprole and iclaprim (for pneumonias). Moreover, all of them would be useful for skin and soft tissue infections.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic activity and resistance of faropenem, dalbavancin, telavancin, ceftobiprole, and iclaprim against skin and soft tissue infections)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



RE.CNT 158 THERE ARE 158 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

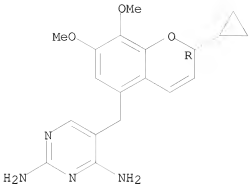
L4 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:892742 CAPLUS
DN 151:353789
TI Evidence based approach to the treatment of community-associated methicillin-resistant Staphylococcus aureus
AU Peppard, William J.; Daniels, Anne; Fehrenbacher, Lynne; Winner, Jamie
CS Froedtert Hospital, Milwaukee, WI, USA
SO Infection and Drug Resistance (2009), 2, 27-40
CODEN: IDRNAV; ISSN: 1178-6973
URL: http://www.dovepress.com/getfile.php?fileID=4936
PB Dove Medical Press (NZ) Ltd.
DT Journal; General Review; (online computer file)
LA English
AB A review. Community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) infections have increased dramatically over the last two decades. The types of infections can range from complicated skin and skin structure infections (cSSSI) to pneumonia and endocarditis. Oral antimicrobial therapy, such as trimethoprim-sulfamethoxazole, clindamycin, long-acting tetracyclines, or linezolid may provide enhanced benefit to those with uncomplicated cutaneous lesions when used in conjunction with incision and drainage in an outpatient setting. However, resistance, susceptibilities, patient-specific circumstances, and adverse effects can impact a healthcare professional's choice of antibiotics. In patients with complicated infections requiring hospitalization or parenteral treatment, vancomycin remains the drug of choice, even though increased resistance and decreased efficacy have crept into clin. practice. Linezolid, quinupristin/dalfopristin, daptomycin, and tigecycline are alternative i.v. agents for the treatment of CA-MRSA. Investigational agents such as dalbavancin, telavancin, oritivancin, iclaprim, ceftobiprole, ceftaroline, and others may expand our therapeutic armamentarium for the treatment of infections caused by CA-MRSA in the future.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(evidence based approach to treatment of community-associated methicillin-resistant Staphylococcus to patients discussed)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



RE.CNT 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

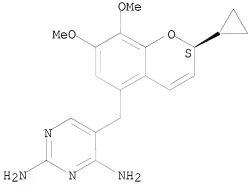
L4 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:884378 CAPLUS
DN 152:254226
TI Inhibitory properties and X-ray crystallographic study of the binding of AR-101, AR-102 and iclaprim in ternary complexes with NADPH and dihydrofolate reductase from Staphylococcus aureus
AU Oefner, Christian; Parisi, Sandro; Schulz, Henk; Lociuro, Sergio; Dale, Glenn E.
CS Arpida Ltd, Reinach, CH-4153, Switz.
SO Acta Crystallographica, Section D: Biological Crystallography (2009), D65(8), 751-757
CODEN: ABCRE6; ISSN: 0907-4449
PB Wiley-Blackwell
DT Journal
LA English
AB Iclaprim is a novel dihydrofolate reductase (DHFR) inhibitor belonging to the 2,4-diaminopyrimidine class of antibiotics, of which trimethoprim (TMP) is the most well known representative. Iclaprim exhibits potent bactericidal activity against major Gram-pos. pathogens, notably methicillin-sensitive Staphylococcus aureus (MSSA) and methicillin-resistant S. aureus (MRSA) phenotypes, including TMP-resistant strains. The inhibition properties of racemic iclaprim and of the two enantiomers, termed AR-101 and AR-102, towards S. aureus wild-type DHFR and TMP-resistant F98Y mutant DHFR were determined and compared. Similar to TMP, AR-101, AR-102 and iclaprim are all competitive inhibitors with respect to the substrate dihydrofolate. Iclaprim, AR-101 and AR-102 demonstrated little or no difference in activity towards these enzymes and were significantly more potent than TMP. The crystal structures of S. aureus DHFR and F98Y mutant DHFR were determined as ternary complexes with NADPH and either AR-101, AR-102 or iclaprim. The binding modes of the inhibitors were analyzed and compared. The X-ray crystallog. data explain the binding modes of all mols. well and can be used to rationalize the equipotent affinity of AR-101, AR-102 and iclaprim, which is also reflected in their antibacterial properties.
IT 1208116-65-7 1208116-66-8
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim, AR-101 and AR-102 than trimethoprim were inhibitors that were one order of magnitude more potent towards wild-type and mutant S. aureus DHFR as evident from X-ray crystallog. data determined as ternary complexes with NADPH)
RN 1208116-65-7 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[[(2R)-2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.

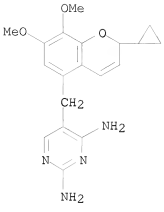


RN 1208116-66-8 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[[(2S)-2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.

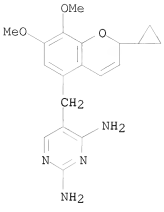


IT 192314-93-5, Iclaprim
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim, AR-101 and AR-102 than trimethoprim were inhibitors that were one order of magnitude more potent towards wild-type and mutant S. aureus DHFR as evident from X-ray crystallog. data determined as ternary complexes with NADPH)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



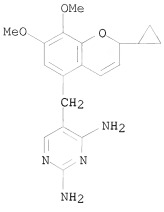
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:831982 CAPLUS
DN 151:93359
TI Multicenter, randomized study of the efficacy and safety of intravenous iclaprim in complicated skin and skin structure infections
AU Krievins, D.; Brandt, R.; Hawser, S.; Hadvary, P.; Islam, K.
CS Stradins Clinical University Hospital, Riga, Latvia
SO Antimicrobial Agents and Chemotherapy (2009), 53(7), 2834-2840
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Iclaprim is a novel antibacterial agent that is currently in development for the treatment of complicated skin and skin structure infections (cSSSI). Iclaprim specifically and selectively inhibits bacterial dihydrofolate reductase, a critical enzyme in the bacterial folate pathway, and exhibits an extended spectrum of activity against various resistant pathogens, including methicillin (methicillin)-resistant Staphylococcus aureus (MRSA). The objective of this randomized, double-blind phase II study was to compare the efficacy and safety of iclaprim to those of vancomycin in patients with cSSSI. Patients were randomized to receive 0.8 mg iclaprim/kg of body weight, 1.6 mg/kg iclaprim, or 1 g vancomycin twice a day for 10 days. Clin. cure rates for the 0.8- and 1.6-mg/kg-iclaprim treatment groups were comparable to that for the vancomycin treatment group (26/28 patients [92.9%], 28/31 patients [90.3%], and 26/28 patients [92.9%], resp.). Iclaprim also showed high microbiol. eradication rates. Iclaprim exhibited an eradication rate of 80% and 72% vs. 59% observed with vancomycin for S. aureus, the pathogen most frequently isolated at baseline. Five MRSA cases were observed, four in the 0.8-mg/kg-iclaprim arm and one in the vancomycin arm, and all were both clin. and microbiol. cured. Iclaprim exhibited a safety profile similar to that of vancomycin, an established drug for the treatment of cSSSI. Results from this study indicate that iclaprim is a promising new therapy for the treatment of cSSSI, in particular those caused by S. aureus, including MRSA.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim against complicated skin and skin structure infections by resistant Staphylococcus aureus and Streptococcus pyogenes)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



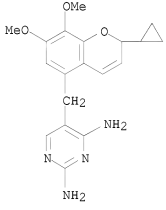
OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:829987 CAPLUS
DN 152:183011
TI Iclaprim, a novel diaminopyrimidine for the treatment of resistant gram-positive infections
AU Sincak, Carrie A.; Schmidt, Justin M.
CS USA
SO Annals of Pharmacotherapy (2009), 43(6), 1107-1114
CODEN: APHRER; ISSN: 1060-0280
PB Harvey Whitney Books Co.
DT Journal; General Review
LA English
AB Objective: To review the pharmacol., microbiol., in vitro susceptibility, pharmacokinetics, clin. trial data, safety, and tolerability of iclaprim, a novel dihydrofolate reductase (DHFR) inhibitor. Data Sources: A MEDLINE search was conducted from 1966 through Dec. 2008. Addnl. sources included abstrs. from meetings of the Interscience Conference on Antimicrobial Agents and Chemotherapy and the Infectious Diseases Society of America from 2001 to 2008 and information available from the manufacturer's Web Site. Study Selection And Data Extraction: In vitro and clin. studies, in addition to Phase 1, 2, and 3 clin. trials, were included. Data Synthesis: Iclaprim, a novel diaminopyrimidine and DHFR antagonist, has a mechanism of action similar to that of trimethoprim. It has in vitro activity mainly against gram-pos. organisms, including resistant Staphylococcus aureus. In Phase 2 and 3 clin. trials, oral and i.v. administration of iclaprim was effective and well tolerated for the treatment of complicated skin and skin structure infections (cSSSI). Trials are currently ongoing for the treatment of ventilator-associated and health-care-associated pneumonia.
Conclusions: Iclaprim is a promising antimicrobial agent for the treatment of gram-pos. organisms, including resistant S. aureus and trimethoprim-, macrolide-, fluoroquinolone-, and glycopeptide-resistant strains. Addnl., in vitro activity similar to that of trimethoprim has been observed against gram-neg. and atypical organisms.
IT 192314-93-5, Iclaprim
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim, novel diaminopyrimidine for treatment of resistant gram-pos. infections)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



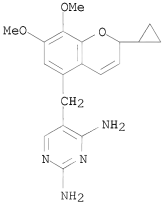
OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:585410 CAPLUS
DN 150:467424
TI Potency and bactericidal activity of iclaprim against recent clinical Gram-positive isolates
AU Sader, Helio S.; Fritsche, Thomas R.; Jones, Ronald N.
CS JMI Laboratories, North Liberty, IA, USA
SO Antimicrobial Agents and Chemotherapy (2009), 53(5), 2171-2175
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB The in vitro activity of iclaprim, a novel diaminopyrimidine derivative, was evaluated against 5,937 recent gram-pos. clin. isolates collected in the United States and Europe. Iclaprim demonstrated potent activity against Staphylococcus aureus (including methicillin-resistant S. aureus [MRSA]), beta-hemolytic Streptococcus spp., and Enterococcus faecalis strains tested. In addition, iclaprim exhibited bactericidal activity against all S. aureus strains tested, including MRSA.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibiotic activity of iclaprim against gram-pos. pathogen)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



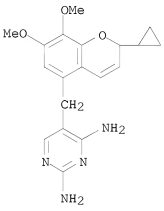
OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:525174 CAPLUS
DN 151:417301
TI Forthcoming therapeutic perspectives for infections due to multidrug-resistant Gram-positive pathogens
AU Cornaglia, G.; Rossolini, G. M.
CS Dipartimento di Patologia, Sezione di Microbiologia, Universita di Verona, Verona, Italy
SO Clinical Microbiology and Infection (2009), 15(3), 218-223
CODEN: CMINFM; ISSN: 1198-743X
PB Wiley-Blackwell
DT Journal; General Review
LA English
AB A review. Multidrug resistance in Gram-pos. pathogens emerged as a major therapeutic challenge over two decades ago. The worldwide spread of methicillin-resistant Staphylococcus aureus (MRSA), glycopeptide-resistant enterococci and other resistant Gram-pos. pathogens had a major impact on antibiotic policies, and prompted the discovery and development of new antibiotics to combat difficult-to-treat infections caused by such pathogens. Several new antibiotics active against multidrug-resistant Gram-pos. pathogens have recently been introduced into clin. practice, and the antibiotic pipeline contains addnl. anti-Gram-pos. drugs at an advanced stage of development, including new glycopeptides (dalbavancin, oritavancin, and telavancin), new anti-MRSA β-lactams (ceftobiprole), and new diaminopyrimidines (iclaprim). This article provides a brief overview of these upcoming agents, partially based on the material presented at the ESCMID Conference entitled 'Fighting infections due to multidrug-resistant Gram-positives' and on the most recent literature.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim may be effective in treatment of patient with infection due to multidrug resistant Staphylococcus aureus or Enterococcus)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



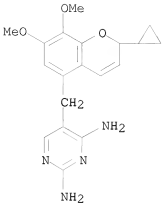
OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:451763 CAPLUS
DN 150:467408
TI In vitro activity of iclaprim against respiratory and bacteremic isolates of Streptococcus pneumoniae
AU Zhanel, George G.; Karlowsky, James A.
CS Department of Medical Microbiology and Infectious Diseases, Faculty of Medicine, University of Manitoba, Winnipeg, MB, Can.
SO Antimicrobial Agents and Chemotherapy (2009), 53(4), 1690-1692
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Iclaprim, a novel dihydrofolate reductase inhibitor, inhibited 90% of the clin. isolates (MIC90) of Streptococcus pneumoniae (n = 785) collected by a national surveillance program at a concentration of 1 μg/mL. The MIC90 for iclaprim was 7 doubling dilns. lower for trimethoprim-sulfamethoxazole-susceptible isolates (n = 670; MIC90, 0.06 μg/mL) than for trimethoprim-sulfamethoxazole-resistant isolates (n = 115; MIC90, ≥8 μg/mL). The potential clin. utility of iclaprim to treat patients with pneumococcal infections may depend upon the current prevalence of resistance to trimethoprim-sulfamethoxazole in this pathogen.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro activity of iclaprim against respiratory and bacteremic isolates of Streptococcus pneumoniae)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:325049 CAPLUS
DN 150:510000
TI Increased hydrophobic interactions of iclaprim with Staphylococcus aureus dihydrofolate reductase are responsible for the increase in affinity and antibacterial activity
AU Oefner, Christian; Bandera, Monica; Haldimann, Andreas; Laue, Heike; Schulz, Henk; Mukhija, Seema; Parisi, Sandro; Weiss, Laurent; Lociuro, Sergio; Dale, Glenn E.
CS Arpida AG, Reinach, CH-4153, Switz.
SO Journal of Antimicrobial Chemotherapy (2009), 63(4), 687-698
CODEN: JACHDX; ISSN: 0305-7453
PB Oxford University Press
DT Journal
LA English
AB Iclaprim is a novel 2,4-diaminopyrimidine that exhibits potent, rapid bactericidal activity against major Gram-pos. pathogens, including methicillin-susceptible Staphylococcus aureus and methicillin-resistant S. aureus, and is currently in clin. development for the treatment of complicated skin and skin structure infections. An understanding of the known mechanism of resistance to trimethoprim led to the design of this new inhibitor, with improved affinity towards dihydrofolate reductase (DHFR) from S. aureus and clin. useful activity against S. aureus including isolates resistant to trimethoprim. The objective of this study was to characterize the mode of action of iclaprim and its inhibitory properties against DHFR. The mode of action of iclaprim was assessed by enzymic anal., direct binding studies, macromol. synthesis profiles, synergy and antagonism studies to define its role as an inhibitor of DHFR. The binding properties of iclaprim to DHFR were compared with those of trimethoprim by X-ray crystallog. The enzymic properties, direct binding and X-ray crystallog. studies delineated the mode of interaction with DHFR and the reason for the increased affinity of iclaprim towards the enzyme. The effect of iclaprim on bacterial physiol. suggests that iclaprim behaves as a classical antibacterial DHFR inhibitor, as previously documented for trimethoprim. Iclaprim binds and inhibits bacterial DHFR in a similar manner to trimethoprim. However, the increased hydrophobic interactions between iclaprim and DHFR account for increased affinity and, unlike trimethoprim, enable iclaprim to inhibit even the resistant enzyme with nanomolar affinity, thus overcoming the mechanism of trimethoprim resistance. The increased antibacterial activity and lower propensity for resistance make iclaprim a clin. promising and useful inhibitor.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(increased hydrophobic interactions of iclaprim with Staphylococcus aureus dihydrofolate reductase are responsible for increase in affinity and antibacterial activity)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)

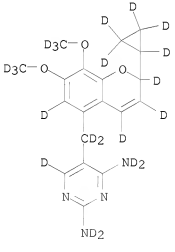


OSC.G 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

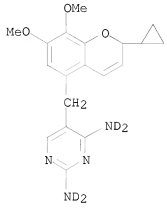
L4 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:292596 CAPLUS
DN 150:313939
TI Deuterium-enriched iclaprim for treating methicillin-resistant Staphylococcus aureus and/or Staphylococcus aureus
IN Czarnik, Anthony W.
PA Protia, LLC, USA
SO U.S. Pat. Appl. Publ., 10pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 20090069357	A1	20090312	US 2008-196599	20080822
PRAI US 2007-970982P	P	20070909		

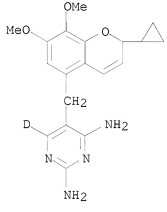
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS MARPAT 150:313939
AB The present application describes deuterium-enriched iclaprim, pharmaceutically acceptable salt forms thereof, and methods of treating using the same. A method is also provided for treating a disease selected from methicillin-resistant Staphylococcus aureus and/or Staphylococcus aureus, comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the deuterium-enriched compds. of the present invention or a pharmaceutically acceptable salt thereof. Various deuterium-enriched iclaprim derivs. are suggested in the examples.
IT 1130072-51-3 1130072-52-4 1130072-54-6
1130072-55-7 1130072-56-8 1130072-57-9
1130072-58-0 1130072-59-1
RL: PRPH (Prophetic); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(deuterium-enriched iclaprim for treating methicillin-resistant Staphylococcus aureus or Staphylococcus aureus)
RN 1130072-51-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



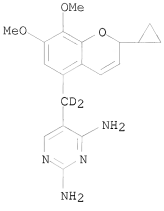
RN 1130072-52-4 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



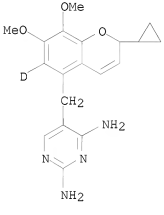
RN 1130072-54-6 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



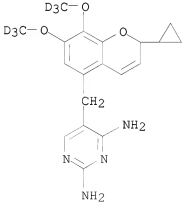
RN 1130072-55-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



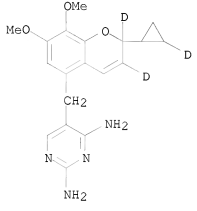
RN 1130072-56-8 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



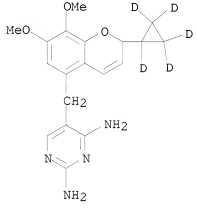
RN 1130072-57-9 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



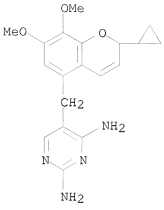
RN 1130072-58-0 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



RN 1130072-59-1 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



IT 192314-93-5D, Iclaprim, deuterium-enriched
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(deuterium-enriched iclaprim for treating methicillin-resistant Staphylococcus aureus or Staphylococcus aureus)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)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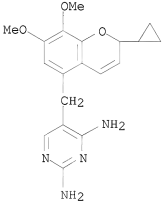
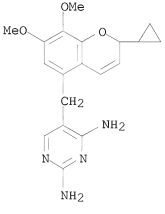
L4 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:271854 CAPLUS
DN 151:259385
TI Iclaprim: a novel dihydrofolate reductase inhibitor for skin and soft tissue infections
AU Morgan, Andrew; Cofer, Christine; Stevens, Dennis L.
CS Veterans Affairs Medical Center, Boise, ID, USA
SO Future Microbiology (2009), 4(2), 131-144
CODEN: FMUIAR; ISSN: 1746-0913
PB Future Medicine Ltd.
DT Journal; General Review
LA English
AB A review. Antibiotic resistance is an ever-increasing concern in the treatment of severe skin and skin-structure infections, pneumonia, bacteremia and other serious infections caused by methicillin-resistant Staphylococcus aureus, vancomycin-resistant S. aureus, group A Streptococcus and vancomycin-resistant Enterococcus. In this review, we summarize the current status of both US FDA-approved and investigational agents aimed at this group of pathogens. We also describe, in detail, the chemical, mechanism of action, pharmacokinetic properties and spectrum of microbiol. activity of iclaprim, a novel dihydrofolate reductase inhibitor recently awarded fast-track approval status by the FDA. Finally, we review the clin. efficacy of iclaprim compared with linezolid for skin and skin-structure infections as demonstrated in Phase III randomized, controlled trials, and comment on its potential role in the treatment of other severe infections with drug-resistant Gram-pos. pathogens.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim was effective in patient with skin and soft tissue infections caused by antibiotic-resistant Gram-pos. organism)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



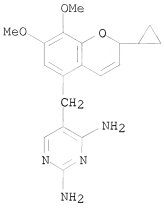
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:226464 CAPLUS
DN 150:255406
TI Activity of iclaprim against clinical isolates of Streptococcus pyogenes and Streptococcus agalactiae
AU Morrissey, I.; Maher, K.; Hawser, S.
CS Microbiology, Quotient Bioresearch Ltd, Fordham, CB7 5WW, UK
SO Journal of Antimicrobial Chemotherapy (2009), 63(2), 413-414
CODEN: JACHDX; ISSN: 0305-7453
PB Oxford University Press
DT Journal
LA English
AB The in vitro activities of iclaprim, trimethoprim/sulfamethoxazole (co-trimoxazole), clarithromycin, clindamycin, linezolid, penicillin G, levofloxacin, and vancomycin against clin. isolates of Streptococcus pyogenes and S. agalactiae were investigated. Iclaprim was more active against S. pyogenes than co-trimoxazole, levofloxacin, linezolid, and vancomycin. Activity against S. agalactiae was higher than those of levofloxacin, linezolid, clarithromycin, and clindamycin and comparable to those of co-trimoxazole, penicillin, and vancomycin. Iclaprim was active against macrolide-resistant isolates of S. pyogenes and agalactiae.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic activity of iclaprim against Streptococcus pyogenes and Streptococcus agalactiae)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



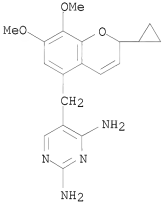
OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:201306 CAPLUS
DN 151:115267
TI What's new and not so new on the antimicrobial horizon?
AU French, G. L.
CS Department of Infection, King's College and Guy's and St Thomas Hospital, London, UK
SO Clinical Microbiology and Infection (2008), 14(Suppl. 6), 19-29
CODEN: CMINFM; ISSN: 1198-743X
PB Wiley-Blackwell
DT Journal; General Review
LA English
AB A review. Despite increasing antimicrobial resistance and multiple drug resistance in clin. isolates of both Gram-pos. and Gram-neg. bacteria, there are few novel antimicrobial agents in development. The few new agents that have been recently licensed have tended to have narrow spectra of activity, focused on Gram-pos. pathogens, especially methicillin-resistant Staphylococcus aureus (MRSA). This situation is rightly causing concern among clinicians and public health authorities worldwide. This article reviews available data on three new antibacterials currently in development. The cephalosporin ceftobiprole is active against MRSA, Enterococcus faecalis and penicillin-resistant Streptococcus pneumoniae, but otherwise has a spectrum of activity similar to that of other recent cephalosporins. In a clin. trial, ceftobiprole was non-inferior to vancomycin for the treatment of MRSA-associated complicated skin and skin structure infections (cSSSIs). Doripenem, a new carbapenem, has some activity against MRSA, but otherwise has an anti-Gram-pos. spectrum of activity similar to that of imipenem and an anti-Gram-neg. spectrum similar to that of meropenem. In a clin. trial, it was non-inferior to meropenem for the treatment of complicated intra-abdominal infections. Iclaprim is a dihydrofolate reductase inhibitor with greatly enhanced activity, as compared with trimethoprim, against a range of Gram-pos. and Gram-neg. pathogens. The limited literature concerning this agent has concentrated on its potential role in the treatment of infections with Gram-pos. bacteria. A clin. trial has demonstrated the non-inferiority of iclaprim, as compared with linezolid, in the treatment of cSSSIs, including those associated with MRSA.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new antibacterial agent iclaprim was useful in treatment of patient with methicillin-resistant Staphylococcus aureus-associated complicated skin and skin structure infection)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



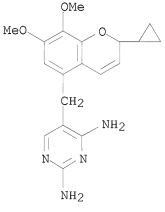
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:199769 CAPLUS
DN 151:331950
TI In vitro activity of iclaprim and comparison agents tested against Neisseria gonorrhoeae including medium growth supplement effects
AU Jones, Ronald N.; Biedenbach, Douglas J.; Sader, Helio S.
CS JMI Laboratories, North Liberty, IA, 52317, USA
SO Diagnostic Microbiology and Infectious Disease (2009), 63(3), 339-341
CODEN: DMIDDZ; ISSN: 0732-8893
PB Elsevier Inc.
DT Journal
LA English
AB Iclaprim is a novel diaminopyrimidine currently in phase III clin. development. This study was conducted to determine the activity of iclaprim compared with trimethoprim and other commonly prescribed drug classes against a comprehensive collection of 156 Neisseria gonorrhoeae, including subsets of organisms resistant to β-lactams and fluoroquinolones (>60%). Iclaprim (MIC50/90, 4/8 μg/mL) was 16-fold more potent than trimethoprim (MIC50/90, 64/>64 μg/mL), and medium growth supplements did not adversely influence activity. Lack of cross-resistances for iclaprim with other commonly used therapies could make iclaprim an alternative for several sexually transmitted diseases (gonococci, Chlamydia trachomatis).
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(N. gonorrhoeae including organism resistant to β-lactams, fluoroquinolones treated by iclaprim, trimethoprim, diverse drug show iclaprim more potent, medium growth supplements not badly influence activity, no cross-resistances with drugs)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



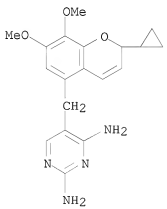
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2008:1504105 CAPLUS
DN 151:94
TI Current and novel antibiotics against resistant Gram-positive bacteria
AU Perez, Federico; Salata, Robert A.; Bonomo, Robert A.
CS Division of Infectious Diseases and HIV Medicine, University Hospitals Case Medical Center, Cleveland, OH, USA
SO Infection and Drug Resistance (2008), 1, 27-44
CODEN: IDRNAV; ISSN: 1178-6973
URL: http://www.dovepress.com/articles.php?article_id=2207
PB Dove Medical Press (NZ) Ltd.
DT Journal; General Review; (online computer file)
LA English
AB A review. The challenge posed by resistance among Gram-pos. bacteria, epitomized by methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus (VRE) and vancomycin-intermediate and -resistant S. aureus (VISA and VRSA) is being met by a new generation of antimicrobials. This review focuses on the new β-lactams with activity against MRSA (ceftobiprole and ceftaroline) and on the new glycopeptides (oritavancin, dalbavancin, and telavancin). It will also consider the role of vancomycin in an era of existing alternatives such as linezolid, daptomycin and tigecycline. Finally, compds. in early development are described, such as iclaprim, friulimicin, and retapamulin, among others.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim may be useful in patient with resistant Gram-pos. bacteria infection)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



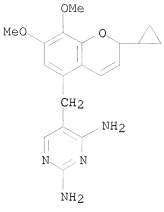
OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
RE.CNT 150 THERE ARE 150 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2008:594822 CAPLUS
DN 149:298726
TI Physicochemical properties of antibacterial compounds: implications for drug discovery
AU O'Shea, Rosemarie; Moser, Heinz E.
CS Achaogen Pharmaceuticals Inc., South San Francisco, CA, 94080, USA
SO Journal of Medicinal Chemistry (2008), 51(10), 2871-2878
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB With the rise of multidrug-resistant pathogens and the need for novel antibiotics, it is critical to understand as much as possible from prior efforts and to apply learned lessons to the discovery of future antibiotics. One important parameter in particular has previously been mentioned but, in the view, not sufficiently analyzed: the physicochem. property space of antibacterial drugs. The authors selected 147 antibacterially active compds. that encompass both currently used drugs and compds. that are still under clin. investigation (see Methods for details). Where available, other property values were extracted from the literature, including protein binding and oral bioavailability in humans. This anal. suggests that natural products should be increasingly investigated again to identify novel antibacterial hits. Besides their high level of structural diversity, they are likely to better cover the required physicochem. property space for antibacterial compds. compared to synthetic mols. because of an increased d. of polar functionalities.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(physicochem. properties of antibacterial compds. and implications for drug discovery)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



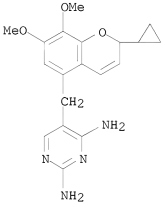
OSC.G 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2008:477514 CAPLUS
DN 148:417108
TI Coagulase-negative staphylococcus infections - antibacterial therapy, therapeutic problems, and novel antibacterial agents
AU Stock, Ingo
CS Bruehl bei Koeln, D-50321, Germany
SO Chemotherapie Journal (2008), 17(1), 10-24
CODEN: CHJOFT; ISSN: 0940-6735
PB Wissenschaftliche Verlagsgesellschaft mbH
DT Journal; General Review
LA German
AB A review. Several coagulase-neg. staphylococcus species are frequent agents of a variety of nosocomial and community-acquired infections, in particular in young children, infants, and in the elderly population. They are the leading agents of nosocomial sepsis in neonates and frequent causes of other blood-stream infections. Endocarditis and meningitis as well as various infections of the urinary tract, soft tissue, wound, eye, and skin are also attributed to these bacteria. The most frequent pathogen of many of these infections is Staphlococcus epidermidis, followed by S. hominis, S. haemolyticus, S. warneri, S. lugdunensis, and S. saprophyticus. Problems concerning the antibacterial treatment of staphylococcus infections arise from strains that have acquired resistances to several agents of different antimicrobial sub-groups, i.e., beta-lactams, aminoglycosides, fluoroquinolones, macrolides, lincosamides, fusidic acid, co-trimoxazole, and other antistaphylococcal agents. Another problem are biofilms that are frequently generated by the bacteria during indwelling medical device associated infections. Bacteria found in biofilms are often poorly controlled by current antistaphylococcal agents. Therefore, novel antibacterial substances with an enhanced activity against multiresistant strains as well as biofilm forming bacteria are strongly required. The currently most promising candidates for the treatment of infections due to coagulase-neg. staphylococci comprise linezolid, tigecycline and ceftobiprole as well as some new glycopeptides, i.e., dalbavancin, oritavancin, and telavancin. Iclaprim, the topical pleuromutilin retapamulin, the quinolone derivate DX-619 and the peptide deformylase inhibitor LBM415 might also represent attractive therapeutic agents and should be considered for further investigation.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibacterial therapy, therapeutic problems, and novel antibacterial agents for coagulase-neg. staphylococcus infections)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



RE.CNT 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2008:363860 CAPLUS
DN 150:486601
TI Iclaprim, a diaminopyrimidine dihydrofolate reductase inhibitor for the potential treatment of antibiotic-resistant staphylococcal infections
AU Peppard, William J.; Schuenke, Christopher D.
CS Froedtert Hospital, Milwaukee, WI, 53226, USA
SO Current Opinion in Investigational Drugs (Thomson Scientific) (2008), 9(2), 210-225
CODEN: COIDAZ; ISSN: 1472-4472
PB Thomson Scientific
DT Journal; General Review
LA English
AB A review. Arpida Ltd, under license from Roche AG, is developing the diaminopyrimidine dihydrofolate reductase inhibitor iclaprim for the potential treatment of methicillin-resistant Staphylococcus aureus infections, including complicated skin and skin structure infections and hospital-acquired pneumonia. Phase III cSSSI clin. trials have been completed and an NDA filing process is ongoing. A phase II clin. trial for hospital-acquired pneumonia is ongoing.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diaminopyrimidine dihydrofolate reductase inhibitor iclaprim may be effective in treatment of patient with methicillin-resistant Staphylococcus aureus including complicated skin and skin structure infection and hospital-acquired pneumonia)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
RE.CNT 140 THERE ARE 140 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2008:223548 CAPLUS
DN 148:269428
TI Once-a-day antibiotic formulations for treatment of methicillin-resistant Staphylococcus aureus infection
IN Flanner, Henry H.; Treacy, Donald; Tolle-Sander, Sanna; Burnside, Beth A.; Rudnic, Edward
PA Middlebrook Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 58pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2008021089	A2	20080221	WO 2007-US17552	20070807
	WO 2008021089	A3	20080821		
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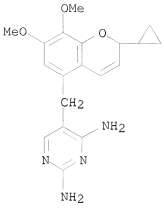
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA		
	US 20100016333	A1	20100121	US 2007-890747	20070807
PRAI	US 2006-836026P	P	20060807		
	US 2006-836313P	P	20060808		

AB Once-a-day oral antibiotic products for treating methicillin-resistant Staphylococcus aureus (MRSA) are provided, comprising a combination of at least 3 different antibiotics selected from RNA polymerase inhibiting antibiotics, phenazine antibiotics, dihydropteroate synthase inhibiting antibiotics, and dihydrofolate reductase inhibiting antibiotics, optionally in combination with a resistance inhibitor, preferably a LexA protease cleavage inhibitor. The product further comprises at least one component(s) selected from the group comprising immediate release components and modified release components, each component comprising a pharmaceutically acceptable carrier and at least one antibiotic. Thus, tablet cores were prepared containing rifapentin 65%, microcryst. cellulose 20%, polyvinylpyrrolidone (K30) 10%, and croscarmellose sodium 5%. Cores 75% were then film coated with 20% Et cellulose and 5% hydroxypropyl cellulose to obtain a one-a-day tablet formulation.

IT 192314-93-5, Iclaprim
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release antibiotic formulations for treatment of methicillin-resistant Staphylococcus aureus infection)

RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)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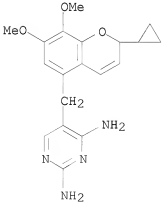
L4 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:1365617 CAPLUS
DN 148:116663
TI Effect of human plasma on the antimicrobial activity of iclaprim in vitro
AU Laue, H.; Valensise, T.; Seguin, A.; Hawser, S.; Lociuro, S.; Islam, K.
CS Arpida AG, Duggingerstrasse 23, Reinach, 4153, Switz.
SO Journal of Antimicrobial Chemotherapy (2007), 60(6), 1388-1390
CODEN: JACHDX; ISSN: 0305-7453
PB Oxford University Press
DT Journal
LA English
AB Iclaprim is a novel diaminopyrimidine for which a human plasma binding level of approx. 93% has been reported. The purpose of this study was to evaluate the effect of human plasma on the in vitro activity of iclaprim and to compare it with that of fusidic acid, teicoplanin and vancomycin, antibiotics with protein binding to human plasma of 97 %, >90 % and 55 %, resp. MICs were determined using 40 methicillin-susceptible Staphylococcus aureus (MSSA) and 38 methicillin-resistant S. aureus (MRSA) isolates in Mueller-Hinton broth (MHB) alone or in the presence of 50 % human plasma. MICs of iclaprim were not affected by the addition of human plasma. MIC ranges (MIC90) for iclaprim against MSSA and MRSA were <0.016-0.06 mg/L (MIC90 0.06 mg/L) and <0.016-0.5 mg/L (MIC90 0.06 mg/L), resp., in MHB and <0.016-0.125 mg/L (MIC90 0.06 mg/L) and <0.016-0.25 mg/L (MIC90 0.125 mg/L), resp., in the presence of human plasma. As expected, the antimicrobial activity of fusidic acid was greatly affected by the presence of human plasma (MIC elevations of 4- to >128-fold), whereas MICs of vancomycin remained unchanged. By contrast, despite the high protein binding, MICs of teicoplanin were only marginally affected by the presence of plasma with an MIC elevation of maximum 8-fold for two strains. This study demonstrates that human plasma does not affect the MIC of iclaprim in vitro.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of human plasma on antimicrobial activity of iclaprim in vitro in comparison with other antibiotics)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



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OSC.G   6     THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
RE.CNT  10    THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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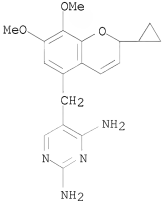
L4 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:1365584 CAPLUS
DN 148:49561
TI In vitro activity of the novel diaminopyrimidine, iclaprim, in combination with folate inhibitors and other antimicrobials with different mechanisms of action
AU Laue, H.; Weiss, L.; Bernardi, A.; Hawser, S.; Lociuro, S.; Islam, K.
CS Arpida AG, Reinach, 4153, Switz.
SO Journal of Antimicrobial Chemotherapy (2007), 60(6), 1391-1394
CODEN: JACHDX; ISSN: 0305-7453
PB Oxford University Press
DT Journal
LA English
AB To assess the synergistic potential of the novel diaminopyrimidine iclaprim (formerly AR-100, Ro 48-2622), a specific and selective inhibitor of microbial dihydrofolate reductase (DHFR), in combination with other antimicrobial agents with distinctly different mechanisms of action. In chequerboard studies, iclaprim was tested in combination with 32 different antimicrobial agents against Gram-pos., Gram-neg. and anaerobic bacteria including reference strains. Iclaprim was highly synergistic against the strains tested with the 2 sulfonamides selected, namely, sulfamethoxazole and sulfadiazine. With the other 28 antimicrobial agents, neither synergy nor antagonism was observed with macrolides, lincosamides, aminoglycosides, quinolones, β-lactams, trimethoprim, tetracyclines and glycopeptides. Furthermore, iclaprim exhibited no synergy or antagonism when evaluated in combination with metronidazole or aztreonam against a panel of 19 bacterial strains, including Gram-pos., Gram-neg. and selected anaerobic bacteria. In agreement with the mechanism of action of microbial DHFR inhibitors, iclaprim exhibited synergism with sulfonamides and exhibited neither antagonism nor synergy with all the other antibiotics tested. Notably, iclaprim exhibited indifference in combination with aztreonam and metronidazole against Gram-negatives and anaerobes, resp.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim antibiotic activity combined with dihydrofolate reductase inhibitors and other antibiotics)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



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OSC.G   13    THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
RE.CNT  10    THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
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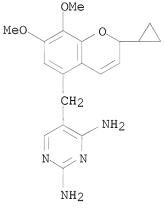
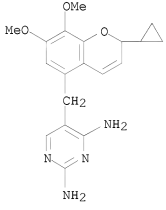
L4 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:1286714 CAPLUS
DN 148:416885
TI Late stage antibacterial drugs in the clinical pipeline
AU Projan, Steven J.; Bradford, Patricia A.
CS Wyeth Research, Cambridge, MA, 02140, USA
SO Current Opinion in Microbiology (2007), 10(5), 441-446
CODEN: COMIF7; ISSN: 1369-5274
PB Elsevier B.V.
DT Journal; General Review
LA English
AB A review. Bacterial resistance to antimicrobial agents is a growing problem worldwide. Not only is issue compounded by the fact that there are fewer pharmaceutical companies conducting research to discover novel antimicrobials than in the past but development time lines have stretched so that a dozen years from discovery to the market is now the standard Eleven antibacterial drugs in late stage clin. development are discussed. Whereas many of these may successfully deal with resistant strains of Gram-pos. pathogens, there is very little in development to address the gorwing unmet medical need of multi-drug resistant Gram-neg. infections.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim showed antibacterial activity against methicillin-resistant Staphylococcus aureus in patient)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



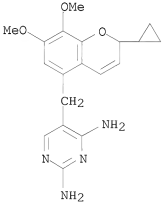
OSC.G 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:1283786 CAPLUS
DN 148:4860
TI Activity of iclaprim against Legionella pneumophila
AU Morrissey, Ian; Hawser, Stephen
CS GR Micro Ltd, London, NW1 3ER, UK
SO Journal of Antimicrobial Chemotherapy (2007), 60(4), 905-906
CODEN: JACHDX; ISSN: 0305-7453
PB Oxford University Press
DT Journal
LA English
AB Iclaprim is a new hydrofolate reductase inhibitor. This antibiotic can be used in combination with sulfonamides against Legionella pneumophila. Iclaprim was very active with 16-fold lower MIC50 or MIC90 than trimethoprim alone. Sulfamthoxazole was inactive and trimethoprim/sulfamethoxazole was also less active than iclaprim. Iclaprim was active similar to clarithromycin, but was less active than levofloxacin.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic activity of iclaprim against Legionella pneumophila)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



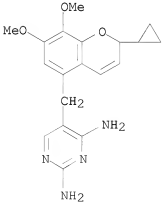
OSC.G 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:1122440 CAPLUS
DN 148:102
TI Alternatives to vancomycin for the treatment of methicillin-resistant Staphylococcus aureus infections
AU Micek, Scott T.
CS Department of Pharmacy, Barnes-Jewish Hospital, St. Louis, MO, USA
SO Clinical Infectious Diseases (2007), 45(Suppl. 3), S184-S190
CODEN: CIDIEL; ISSN: 1058-4838
PB University of Chicago Press
DT Journal; General Review
LA English
AB A review. Vancomycin remains the reference standard for the treatment of systemic infection caused by methicillin-resistant Staphylococcus aureus (MRSA). However, as a result of limited tissue distribution, as well as the emergence of isolates with reduced susceptibility and in vitro resistance to vancomycin, the need for alternative therapies that target MRSA has become apparent. New treatment options for invasive MRSA infections include linezolid, daptomycin, tigecycline, and quinupristin/dalfopristin. Addnl., a number of new anti-MRSA compds. are in development, including novel glycopeptides (dalbavancin, telavancin, and oritavancin), ceftobiprole, and iclaprim. The present article will review clin. issues surrounding the newly marketed and investigational agents with activity against MRSA.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iclaprim was used as alternative to vancomycin for treatment of patient with methicillin-resistant Staphylococcus aureus infection)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



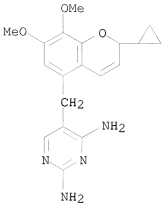
OSC.G 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:930862 CAPLUS
DN 147:356140
TI Iclaprim
AU Kohlhoff, Stephan A.; Sharma, Roopali
CS Division of Pediatric Infectious Diseases, Department of Pediatrics, State University of New York Downstate Medical Center, Brooklyn, NY, 11203, USA
SO Expert Opinion on Investigational Drugs (2007), 16(9), 1441-1448
CODEN: EOIDER; ISSN: 1354-3784
PB Informa Healthcare
DT Journal; General Review
LA English
AB A review. Iclaprim is a novel diaminopyrimidine, and an inhibitor of dihydrofolate reductase, which has shown potent, extended-spectrum in vitro activity against Gram-pos. bacteria, including methicillin-resistant Staphylococcus aureus, vancomycin-intermediate and vancomycin-resistant S. aureus and macrolide-, quinolone- and trimethoprim-resistant strains. In addition, iclaprim has demonstrated activity against Streptococcus pneumoniae including penicillin-, erythromycin-, levofloxacin- and trimethoprim/sulfamethoxazole-resistant strains. Furthermore, in vitro activity has also been observed against Gram-neg. bacteria and atypical bacteria. The pharmacokinetic profile of this agent reveals that iclaprim is available for i.v. and oral use, with good oral bioavailability. Phase II clin. trials have shown promise in its use for complicated skin and skin structure infections that are caused by methicillin-resistant S. aureus and two Phase III clin. trials have been recently completed for the same indication. Phase II trials evaluating the efficacy in respiratory infections are expected to start in 2007. At this early point in clin. development, the available reported data indicate potential for iclaprim as a new antibiotic for parenteral and oral treatment of complicated skin and skin structure infections.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibacterial action of iclaprim against antibiotic resistant bacteria)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



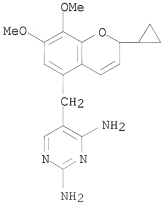
OSC.G 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:924571 CAPLUS
DN 147:377512
TI Concentrations in plasma, epithelial lining fluid, alveolar macrophages and bronchial mucosa after a single intravenous dose of 1.6 mg/kg of iclaprim (AR-100) in healthy men
AU Andrews, J.; Honeybourne, D.; Ashby, J.; Jevons, G.; Fraise, A.; Fry, P.; Warrington, S.; Hawser, S.; Wise, R.
CS Department of Medical Microbiology, City Hospital NHS Trust, Birmingham, UK
SO Journal of Antimicrobial Chemotherapy (2007), 60(3), 677-680
CODEN: JACHDX; ISSN: 0305-7453
PB Oxford University Press
DT Journal
LA English
AB Objectives: A validated microbiol. assay was used to measure concns. of iclaprim (AR-100) in plasma, bronchial mucosa (BM), alveolar macrophages (AM) and epithelial lining fluid (ELF) after a single 1.6 mg/kg i.v. 60 min iv infusion of iclaprim. Methods: Male volunteers were randomly allocated to three nominal sampling time intervals 1-2 h (Group A), 3-4 h (Group B) and 5.57.0 h (Group C) after the start of the drug infusion. Results: Mean iclaprim concns. in plasma, BM, AM and ELF, resp., were for Group A 0.59 mg/L (SD 0.18), 0.51 mg/kg (SD 0.17), 24.51 mg/L (SD 21.22) and 12.61 mg/L (SD 7.33); Group B 0.24 mg/L (SD 0.05), 0.35 mg/kg (SD 0.17), 7.16 mg/L (SD 1.91) and 6.38 mg/L (SD 5.17); and Group C 0.14 mg/L (SD 0.05), no detectable level in BM, 5.28 mg/L (SD 2.30) and 2.66 mg/L (SD 2.08). Conclusions: Iclaprim concns. in ELF and AM exceeded the MIC90 for penicillin-susceptible Streptococcus pneumoniae (MIC90 0.06 mg/L), penicillin-intermediate S. pneumoniae (MIC90 2 mg/L), penicillin-resistant S. pneumoniae (MIC90 4 mg/L) for 7, 7 and 4 h, resp., and Chlamydia pneumoniae (MIC90 0.5 mg/L) for 7 h. Mean iclaprim concns. in ELF exceeded the MIC90 for Haemophilus influenzae (MIC90 4 mg/L) and Moraxella catarrhalis (MIC90 8 mg/L) for up to 4 and 2 h, resp.; in AM the MIC90 was exceeded for up to 7 h. Furthermore, the MIC90 for methicillin-resistant Staphylococcus aureus of 0.12 mg/L was exceeded at all sites for up to 7 h. These data suggest that iclaprim reaches lung concns. that should be effective in the treatment of community-acquired pneumonia.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(concns. in plasma, epithelial lining fluid, alveolar macrophages and bronchial mucosa after single i.v. dose of iclaprim)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

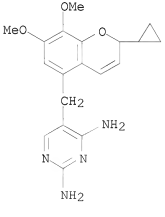
L4 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:901704 CAPLUS
DN 147:421821
TI Crystal Structure of the Anthrax Drug Target, Bacillus anthracis Dihydrofolate Reductase
AU Bennett, Brad C.; Xu, Hai; Simmerman, Richard F.; Lee, Richard E.; Dealwis, Chris G.
CS Department of Biochemistry, Cellular Molecular Biology, University of Tennessee, Knoxville, TN, 37996, USA
SO Journal of Medicinal Chemistry (2007), 50(18), 4374-4381
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Spores of Bacillus anthracis are the infectious agent of anthrax. Current antibiotic treatments are limited due to resistance and patient age restrictions; thus, addnl. targets for therapeutic intervention are needed. One possible candidate is dihydrofolate reductase (DHFR), a biosynthetic enzyme necessary for anthrax pathogenicity. We determined the crystal structure of DHFR from B. anthracis (baDHFR) in complex with methotrexate (MTX; 1) at 2.4 Å resolution The structure reveals the crucial interactions required for MTX binding and a putative mol. basis for how baDHFR has natural resistance to trimethoprim (TMP; 2). The structure also allows insights for designing selective baDHFR inhibitors that will have weak affinities for the human enzyme. Addnl., we have found that 5-nitro-6-methylamino-isocytosine (MANIC; 3), which inhibits another B. anthracis folate synthesis enzyme, dihydropteroate synthase (DHPS), can also inhibit baDHFR. This provides a starting point for designing multi-target inhibitors that are less likely to induce drug resistance.
IT 192314-93-5D, complexes with dihydrofolate reductase
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(crystal structure of Bacillus anthracis dihydrofolate reductase)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:80204 CAPLUS
DN 146:134455
TI Investigational treatments for postoperative surgical site infections
AU Poulakou, Garyphallia; Giamarellou, Helen
CS University General Hospital Attikon, 4th Department of Internal Medicine, National and Kapodistrian University of Athens Medical School, Athens, 12462, Greece
SO Expert Opinion on Investigational Drugs (2007), 16(2), 137-155
CODEN: EOIDER; ISSN: 1354-3784
PB Informa Healthcare
DT Journal; General Review
LA English
AB A review. Surgical site infections rank third among nosocomial infections, representing a global threat, associated with the emergence of multi-drug-resistant bacteria. The pharmaceutical industry has recently curtailed developmental programs; however, the need for new compds. is extremely important. This article reviews new antimicrobials and immunointerventional targets for their potential to treat surgical site infections in comparison with recently licensed compds. Daptomycin, dalbavancin, oritavancin, telavancin, iclaprim and ranbezolid seem to be promising agents against infections caused by Gram-pos. pathogens and effectively address the present problems of multi-resistance in Gram-pos. infections. Peptide deformylase inhibitors and immunostimulating agents open new perspectives in this field; however, very few compds. targeting Gram-neg. problematic pathogens are in the pipeline of the future. Tigecycline (recently marketed) ceftobiprole, ceftaroline and doripenem seem to possess an extended anti-Gram-pos. and -neg. spectrum. Among these compds., only doripenem demonstrates activity against Pseudomonas aeruginosa, for which there is a clear unmet need for new compds., focusing on new targets.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(investigational treatments for postoperative surgical site infections)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

RE.CNT 157 THERE ARE 157 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2006:847676 CAPLUS
DN 145:271796
TI Processes for the preparation of pyrimidinylmethyl 2H-chromenes
IN Schneider, Peter; Tahtaoui, Chouaib
PA Arpida AG, Switz.
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

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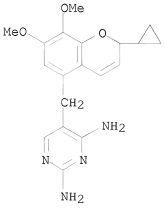
PRAI	WO 2005-EP1695	A	20050218		
	WO 2000-EP2006001695	A	20050218		
	WO 2006-EP1185	W	20060210		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS CASREACT 145:271796; MARPAT 145:271796
AB A process for the preparation of title compds. of formula I comprising reacting a compound of formula II [R = CMe3 or CHMe2] with cyclopropyl Me ketone is disclosed. For example, I was provided in a multi-step synthesis starting from the reaction of trimethoprim with pivalic anhydride.
IT 192314-93-5P, 5-[(2-Cyclopropyl-7,8-dimethoxy-2H-chromen-5-yl)methyl]pyrimidine-2,4-diamine
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of 5-[(2,4-diaminopyrimidinyl)methyl]-2H-chromenes and their intermediates)

RN 192314-93-5 CAPLUS

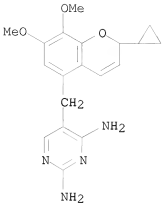
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

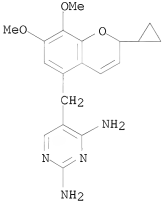
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2006:621823 CAPLUS
DN 146:18974
TI Infections associated with orthopedic implants
AU Trampuz, Andrej; Widmer, Andreas F.
CS Division of Infectious Diseases and Hospital Epidemiology, University Hospital, Basel, Switz.
SO Current Opinion in Infectious Diseases (2006), 19(4), 349-356
CODEN: COIDE5; ISSN: 0951-7375
PB Lippincott Williams & Wilkins
DT Journal; General Review
LA English
AB Purpose of review: We review recent advances in the prevention, diagnosis and treatment of infections associated with joint prostheses and internal fixation devices. Recent findings: The perioperative antimicrobial prophylaxis should be administered 60-30 min before incision or before inflation of the tourniquet. New diagnostic approaches include sonication of removed implants to dislodge adherent microorganisms growing in biofilms and the use of mol. techniques to improve diagnostic yield. Treatment of implant-associated infections without removal of the device is an established option for selected patients. Treatment with rifampin combinations in staphylococcal infections is crucial for success. As demonstrated in vitro, in animal studies and in clin. trials, quinolones are suitable combination agents with rifampin against susceptible staphylococci, but increasing antimicrobial resistance requires evaluation of alternative combination agents, such as quinupristin-dalfopristin, linezolid, and daptomycin, although clin. experience is limited. New antimicrobial agents, such as dalbavancin, tigecycline, iclaprim, and novel rifamycin derivs. are studied. Summary: Better understanding of the interaction between microorganisms, the implant and the host may improve our current approach to the diagnosis and treatment of implant-associated infections. The treatment modality depends on duration of infection, stability of the implant, antimicrobial susceptibility of the pathogen and condition of the surrounding soft tissue.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of rifampin, quinolone, quinupristin, dalfopristin, linezolid, daptomycin, dalbavancin, tigecycline, iclaprim are useful in treatment of orthopedic implant-associated Staphylococcal, other bacterial infections)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



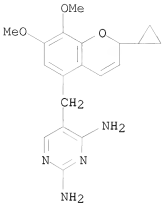
OSC.G 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2006:206090 CAPLUS
DN 144:324015
TI Dihydrofolate reductase inhibitors as antibacterial agents
AU Hawser, Stephen; Lociuro, Sergio; Islam, Khalid
CS Arpida Ltd., Muenchenstein, 4142, Switz.
SO Biochemical Pharmacology (2006), 71(7), 941-948
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier B.V.
DT Journal; General Review
LA English
AB A review. Although only a few DHFR inhibitors have progressed as antibiotics to the market there is much renewed interest in the discovery and development of new generation DHFR inhibitors as antibacterial agents. This article describes the success in exploiting DHFR as a drugable target as exemplified by trimethoprim (TMP) and the development of several new diaminopyrimidines. Iclaprim, a recent example of a novel diaminopyrimidine currently in Phase III clin. trials, is also described together with several examples of anti-DHFR antibacterial compds. in pre-clin. development.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dihydrofolate reductase inhibitors as antibacterial agents)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 51 THERE ARE 51 CAPLUS RECORDS THAT CITE THIS RECORD (51 CITINGS)
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2005:1032155 CAPLUS
DN 144:141511
TI Recently approved and investigational antibiotics for treatment of severe infections caused by Gram-positive bacteria
AU Appelbaum, Peter C.; Jacobs, Michael R.
CS Department of Pathology, Hershey Medical Center, Hershey, PA, 17033, USA
SO Current Opinion in Microbiology (2005), 8(5), 510-517
CODEN: COMIF7; ISSN: 1369-5274
PB Elsevier Ltd.
DT Journal; General Review
LA English
AB A review. The development of resistance in the major pathogenic Gram-pos. genera Staphylococcus and Streptococccus has led to the need for new agents that are able to overcome existing resistance mechanisms or that have novel mechanisms of action. There is currently a dearth of new agents that are active against resistant bacterial species. Agents that have recently been approved for clin. use include linezolid, the first oxazolidinone in clin. use, daptomycin, the first lipopeptide in clin. use, and telithromycin, a ketolide that is derived from clarithromycin. Agents currently in clin. development include tigecycline, a broad-spectrum i.v. tetracycline, ceftobiprole, a broad-spectrum cephalosporin that has activity against methicillin-resistant staphylococci, DX-619 and WCK-771, which are potent quinolones that have activity against quinolone-resistant staphylococci, oritavancin and dalbavancin, both of which are new glycopeptides, and iclaprim, which is a diaminopyrimidine. Addnl. agents that are in preclin. development against Gram-pos. pathogens include quinoline-naphthyridine agents, which target novel DNA gyrase sites, other novel quinolones that have high potency, peptide deformylase inhibitors, and new lincosamide, oxazolidinone, lipopeptide and cephalosporin derivs. Misuse of potent new agents will, however, result in the inevitable development of resistance to these agents; responsible use of potent new agents is required to prevent continuation of this vicious cycle.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diaminopyrimidine iclaprim treatment might be useful for treatment for Gram pos. Staphylococcus, Streptococccus bacterial infection)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 37 THERE ARE 37 CAPLUS RECORDS THAT CITE THIS RECORD (37 CITINGS)
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2005:141063 CAPLUS
DN 142:240455
TI Novel processes and intermediates for the preparation of 2H-chromenes, particularly the antibiotic iclaprim
IN Jaeger, Juergen; Burri, Kaspar; Greiveldinger-Poenaru, Sorana; Hoffner, Johannes
PA Arpida A.-G., Switz.
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005014586	A1	20050217	WO 2003-EP8814	20030808
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	WO 2005014587	A1	20050217	WO 2004-EP8682	20040803
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1656369	A1	20060517	EP 2004-763740	20040803
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	CN 1832942	A	20060913	CN 2004-80022787	20040803
	JP 2007501771	T	20070201	JP 2006-522311	20040803
	HU 2006000231	A2	20080428	HU 2006-231	20040803
	IN 2006CN00478	A	20070706	IN 2006-CN478	20060206
	KR 2006056375	A	20060524	KR 2006-702680	20060208
	NO 2006000643	A	20060220	NO 2006-643	20060209
	US 20080015354	A1	20080117	US 2007-567558	20070406
PRAI	WO 2003-EP8814	A	20030808		
	WO 2004-EP8682	W	20040803		

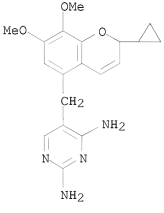
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS CASREACT 142:240455
AB The invention concerns a novel process for the preparation of 2H-chromenes, particularly the antibiotic (no data) iclaprim (I) and a key intermediate (II), and also two valuable intermediates in the processes. Thus, II was prepared in 4 steps from 3-hydroxy-4,5-dimethoxybenzoic acid Me ester via (1) cyclocondensation with cis-(3,3-dimethoxyprop-1-enyl)cyclopropane, (2) alkaline sapon of the ester, (3) reduction of the acid to an alc. with LiAlH4 or Red-Al, and (4) oxidation of the alc. to an aldehyde using SO3-pyridine complex and Et3N in DMSO. Alternatively, II was prepared directly from 3-hydroxy-4,5-dimethoxybenzaldehyde and cis-(3,3-dimethoxyprop-1-enyl)cyclopropane. Condensation of II with

PhNHCH2CH2CN in DMSO in the presence of KOBu-tert gave a cis/trans mixture of PhNHCH:C(CN)R [R = (2-cyclopropyl-7,8-dimethoxy-2H-chromen-5-yl)methyl], which was cyclocondensed with guanidine HCl to give I. Advantages of the new method include use of bulk com. starting materials, avoidance of halogenated solvents, and crystalline and/or non-isolated intermediates.

IT 192314-93-5P, Iclaprim
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of the antibiotic iclaprim and intermediates)

RN 192314-93-5 CAPLUS

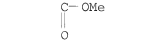
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



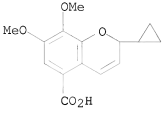
IT 192315-05-2P, 2-Cyclopropyl-7,8-dimethoxy-2H-chromene-5-carboxylic acid methyl ester 845276-37-1P, 2-Cyclopropyl-7,8-dimethoxy-2H-chromene-5-carboxylic acid 845276-38-2P, (2-Cyclopropyl-7,8-dimethoxy-2H-chromene-5-yl)methanol
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process intermediate; preparation of the antibiotic iclaprim and intermediates)

RN 192315-05-2 CAPLUS

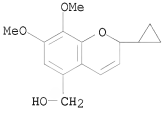
CN 2H-1-Benzopyran-5-carboxylic acid, 2-cyclopropyl-7,8-dimethoxy-, methyl ester (CA INDEX NAME)



RN 845276-37-1 CAPLUS
CN 2H-1-Benzopyran-5-carboxylic acid, 2-cyclopropyl-7,8-dimethoxy- (CA INDEX NAME)

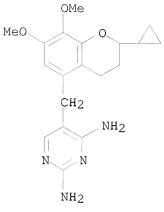


RN 845276-38-2 CAPLUS
CN 2H-1-Benzopyran-5-methanol, 2-cyclopropyl-7,8-dimethoxy- (CA INDEX NAME)



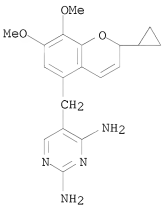
OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2004:566933 CAPLUS
DN 141:270985
TI Three-Dimensional Quantitative Structure-Activity Relationship Analysis of a Set of Plasmodium falciparum Dihydrofolate Reductase Inhibitors Using a Pharmacophore Generation Approach
AU Parenti, Marco Daniele; Pacchioni, Sara; Ferrari, Anna Maria; Rastelli, Giulio
CS Dipartimento di Scienze Farmaceutiche, Universita di Modena e Reggio Emilia, Modena, 41100, Italy
SO Journal of Medicinal Chemistry (2004), 47(17), 4258-4267
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A 3D pharmacophore model able to quant. predict inhibition consts. was derived for a series of inhibitors of Plasmodium falciparum dihydrofolate reductase (PfDHFR), a validated target for antimalarial therapy. The data set included 52 inhibitors, with 23 of these comprising the training set and 29 an external test set. The activity range, expressed as Ki, of the training set mols. was from 0.3 to 11 300 nM. The 3D pharmacophore, generated with the HypoGen module of Catalyst 4.7, consisted of two hydrogen bond donors, one pos. ionizable feature, one hydrophobic aliphatic feature, and one hydrophobic aromatic feature and provided a 3D-QSAR model with a correlation coefficient of 0.954. Importantly, the type and spatial location of the chemical features encoded in the pharmacophore were in full agreement with the key binding interactions of PfDHFR inhibitors as previously established by mol. modeling and crystallog. of enzyme-inhibitor complexes. The model was validated using several techniques, namely, Fisher's randomization test using CatScramble, leave-one-out test to ensure that the QSAR model is not strictly dependent on one particular compound of the training set, and activity prediction in an external test set of compds. In addition, the pharmacophore was able to correctly classify as active and inactive the dihydrofolate reductase and aldose reductase inhibitors extracted from the MDDR database, resp. This test was performed to challenge the predictive ability of the pharmacophore with two classes of inhibitors that target very different binding sites. Mol. diversity of the data sets was finally estimated by the Tanimoto approach. The results obtained provide confidence for the utility of the pharmacophore in the virtual screening of libraries and databases of compds. to discover novel PfDHFR inhibitors.
IT 756887-17-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(QSAR of Plasmodium falciparum dihydrofolate reductase inhibitors using pharmacophore generation approach)
RN 756887-17-9 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-3,4-dihydro-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



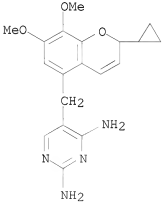
OSC.G 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS RECORD (22 CITINGS)
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2004:375664 CAPLUS
DN 141:85429
TI In vitro activity of a novel diaminopyrimidine compound, iclaprim, against Chlamydia trachomatis and C. pneumoniae
AU Kohlhoff, S. A.; Roblin, P. M.; Reznik, T.; Hawser, S.; Islam, K.; Hammerschlag, M. R.
CS Dep. Pediatrics, Downstate Medical Center, State Univ. New York, Brooklyn, NY, 11203-2098, USA
SO Antimicrobial Agents and Chemotherapy (2004), 48(5), 1885-1886
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB The in vitro activities of iclaprim, a novel dihydrofolate reductase inhibitor, azithromycin, and levofloxacin were tested against 10 strains of C. trachomatis and 10 isolates of Chlamydia pneumoniae. For C. trachomatis and C. pneumoniae, the iclaprim MIC and minimal bactericidal concentration at which 90% of isolates were inhibited (MIC90 and MBC90) were 0.5 μg/mL, compared to an azithromycin MIC90 and MBC90 of 0.125 μg/mL and levofloxacin MIC90s and MBC90s of 1 μg/mL for C. trachomatis and 0.5 μg/mL for C. pneumoniae.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro activity of iclaprim against Chlamydia trachomatis and C. pneumoniae)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

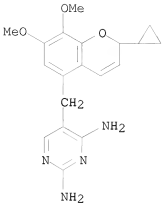
L4 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2004:373800 CAPLUS
DN 141:166971
TI Iclaprim: Antibacterial dihydrofolate reductase inhibitor
AU Sorbera, L. A.; Castaner, J.; Rabasseda, X.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2004), 29(3), 220-225
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review. The need for potent antibacterial agents with novel mechanisms of action remains a research priority. Dihydrofolate reductase (DHFR) is an enzyme essential for bacterial survival that is an excellent target for antibacterial drug development. Diaminopyrimidines such as trimethoprim (TMP) are inhibitors of DHFR which have been used clin. as monotherapy and in combination with other agents with relative success. However, TMP is weakly bactericidal and resistance has emerged due to frequent use. Researchers have therefore focused on the discovery of synthetic derivs. of benzyldiaminopyrimidines which exhibit improved potency and selectivity and can overcome resistance. Iclaprim (I) is a novel diaminopyrimidine that has shown potent, expanded-spectrum activity against Gram-pos. bacteria including methicillin-resistant Staphylococcus aureus, vancomycin-intermediate and vancomycin-resistant S. aureus and macrolide-, quinolone- and TMP-resistant strains. Activity was also observed against Gram-pos. and Gram-neg. pathogens involved in respiratory tract infections and it proved effective in animal models of infection. Moreover, in a phase II trial, I was shown to be safe and effective as a treatment for complicated skin and soft tissue infections.
IT 192314-93-5P, Iclaprim
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antibacterial activity of the dihydrofolate reductase inhibitor iclaprim)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

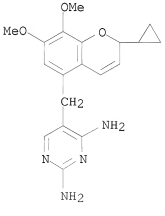
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2004:54705 CAPLUS
DN 140:232383
TI Vancomycin-resistant Staphylococcus aureus isolate from a patient in Pennsylvania
AU Tenover, Fred C.; Weigel, Linda M.; Appelbaum, Peter C.; McDougal, Linda K.; Chaitram, Jasmine; McAllister, Sigrid; Clark, Nancye; Killgore, George; O'Hara, Caroline M.; Jevitt, Laura; Patel, Jean B.; Bozdogan, Buelent
CS Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, GA, 30333, USA
SO Antimicrobial Agents and Chemotherapy (2004), 48(1), 275-280
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB A vancomycin-resistant Staphylococcus aureus (VRSA) isolate was obtained from a patient in Pennsylvania in Sept. 2002. Species identification was confirmed by standard biochem. tests and anal. of 16S ribosomal DNA, gyrA, and gyrB sequences; all of the results were consistent with the S. aureus identification. The MICs of a variety of antimicrobial agents were determined by broth microdilution and macrodilution methods following National Committee for Clin. Laboratory Stds. (NCCLS) guidelines. The isolate was resistant to vancomycin (MIC = 32 μg/mL), aminoglycosides, β-lactams, fluoroquinolones, macrolides, and tetracycline, but it was susceptible to linezolid, minocycline, quinupristin-dalfopristin, rifampin, teicoplanin, and trimethoprim-sulfamethoxazole. The isolate, which was originally detected by using disk diffusion and a vancomycin agar screen plate, was vancomycin susceptible by automated susceptibility testing methods. Pulsed-field gel electrophoresis (PFGE) of SmaI-digested genomic DNA indicated that the isolate belonged to the USA100 lineage (also known as the New York/Japan clone), the most common staphylococcal PFGE type found in hospitals in the United States. The VRSA isolate contained two plasmids of 120 and 4 kb and was pos. for mecA and vanA by PCR amplification. The vanA sequence was identical to the vanA sequence present in Tn1546. A DNA probe for vanA hybridized to the 120-kb plasmid. This is the second VRSA isolate reported in the United States.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vancomycin-resistant Staphylococcus aureus isolate from patient in Pennsylvania)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 161 THERE ARE 161 CAPLUS RECORDS THAT CITE THIS RECORD (161 CITINGS)
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

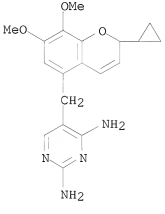
L4 ANSWER 43 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2003:883789 CAPLUS
DN 141:20308
TI Antibacterial susceptibility of a vancomycin-resistant Staphylococcus aureus strain isolated at the Hershey Medical Center
AU Bozdogan, Buelent; Esel, Duygu; Whitener, Cynthia; Browne, Frederick A.; Appelbaum, Peter C.
CS Department of Pathology, Hershey Medical Center, Hershey, PA, 17033, USA
SO Journal of Antimicrobial Chemotherapy (2003), 52(5), 864-868
CODEN: JACHDX; ISSN: 0305-7453
PB Oxford University Press
DT Journal
LA English
AB Staphylococcus aureus strain HMC3 isolated at the Hershey Medical Center, was resistant to vancomycin (VRSA) through the presence of the vanA resistance gene; it also contained mecA, erm(A), erm(B), tet(K) and aac(6')-aph(2''), conferring resistance to licensed β-lactams, macrolides, tetracycline and aminoglycosides. HMC3 also had alterations in GyrA and GrlB and was resistant to available quinolones. Exptl. drugs with low MICs (<2 mg/L) for VRSA HMC3 included cephalosporins BAL9141 and RWJ-54428; glycopeptides oritavancin and dalbavancin; the lipopeptide daptomycin; the glycolipodepsipeptide ramoplanin; new fluoroquinolones WCK 771 A, WCK 1153, DK-507k and sitafloxacin; and the DNA nanobinder GS02-02. These agents were all bactericidal as were trimethoprim/sulfamethoxazole and teicoplanin (MIC 4 mg/L). Oxazolidinones linezolid and ranbezolid; the injectable streptogramin quinupristin/dalfopristin; DNA nanobinders GS2-10547 and GS02-104; peptide deformylase inhibitors NVP-PDF713 and GS02-12; tetracycline derivative tigecycline; the antifolate iclaprim; mupirocin and fusidic acid were all active in vitro but bacteriostatic.
IT 192314-93-5, Iclaprim
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibacterial susceptibility of a vancomycin-resistant Staphylococcus aureus strain isolated at the Hershey Medical Center)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 109 THERE ARE 109 CAPLUS RECORDS THAT CITE THIS RECORD (109 CITINGS)
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

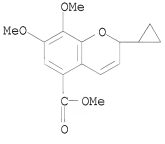
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2003:877316 CAPLUS
DN 140:122159
TI Iclaprim, a novel diaminopyrimidine with potent activity on trimethoprim sensitive and resistant bacteria
AU Schneider, Peter; Hawser, Stephen; Islam, Khalid
CS Arpida Ltd., Muenchenstein, CH-4142, Switz.
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(23), 4217-4221
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
AB Iclaprim, a new selective dihydrofolate inhibitor was synthesized based on rational drug design. Iclaprim's interaction with a resistant Staphylococcus aureus dihydrofolate reductase (DHFR) is outlined in comparison to trimethoprim (TMP). This compound is active against methicillin, TMP and vancomycin resistant strains. Arpida Ltd. is developing Iclaprim for serious hospital infections from Gram-pos. pathogens and respiratory tract infections.
IT 192314-93-5, Iclaprim
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Iclaprim, a novel diaminopyrimidine with potent activity on trimethoprim sensitive and resistant bacteria)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 52 THERE ARE 52 CAPLUS RECORDS THAT CITE THIS RECORD (53 CITINGS)
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

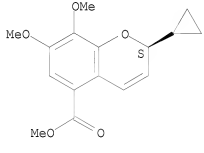
L4 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2003:827746 CAPLUS
DN 140:59491
TI Pt(IV)-catalyzed cyclization of arene-alkyne substrates via C-H bond functionalization
AU Pastine, Stefan J.; Youn, So Won; Sames, Dalibor
CS Department of Chemistry, Columbia University, New York, NY, 10027, USA
SO Tetrahedron (2003), 59(45), 8859-8868
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science B.V.
DT Journal
LA English
OS CASREACT 140:59491
AB PtCl4 was proven to be a hydroarylation catalyst with an efficiency and substrate scope superior to previously reported methods. This catalyst showed consistent performance with arene-yne substrates of diverse structural features, including propargyl ethers, propargylamines, and alkynoate esters, providing good to excellent yields of the 6-endo products, chromenes, e.g., I, dihydroquinolines, e.g., II, and coumarins, e.g., III. Pt(II), Pd(II), and Ga(III) salts were shown to be sensitive to the substitution on the alkyne moiety. PtCl4 is compatible with both terminal and disubstituted alkynes, as well as with various functionalities on the arene ring, including Me, methoxy, hydroxy, protected amine, and halide.
IT 192315-05-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of chromenes via platinum-catalyzed intramol. cyclization of aryloxyalkynes)
RN 192315-05-2 CAPLUS
CN 2H-1-Benzopyran-5-carboxylic acid, 2-cyclopropyl-7,8-dimethoxy-, methyl ester (CA INDEX NAME)



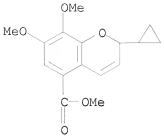
OSC.G 68 THERE ARE 68 CAPLUS RECORDS THAT CITE THIS RECORD (69 CITINGS)
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1999:381749 CAPLUS
DN 131:144499
TI Enantioselective synthesis and photoracemization studies of (+)-2-cyclopropyl-7,8-dimethoxy-2H-chromene-5-carboxylic acid methyl ester, an advanced intermediate of a dihydrofolate reductase inhibitor
AU Wipf, Peter; Weiner, Warren S.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Journal of Organic Chemistry (1999), 64(14), 5321-5324
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 131:144499
AB In a formal asym. synthesis of the potent dihydrofolate reductase inhibitor cyclopropyl(pyrimidinylmethyl)benzopyran I, the enantioenriched building block cyclopropylbenzopyran (S)-II was obtained in 7 steps and in 21% overall yield from 3-hydroxy-4,5-dimethoxybenzoic acid. A caveat in the preparation and pharmaceutical use of chromenes of type II is their surprisingly facile photoracemization at the stereocenter next to the chromene oxygen. The half-lives for racemization of a solution of II in a pyrex flask can be as short as 16 h. This is the first kinetic anal. of chromene photo-racemization.
IT 236393-00-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enantioselective synthesis and photoracemization of cyclopropylchromenecarboxylate)
RN 236393-00-3 CAPLUS
CN 2H-1-Benzopyran-5-carboxylic acid, 2-cyclopropyl-7,8-dimethoxy-, methyl ester, (2S)- (CA INDEX NAME)

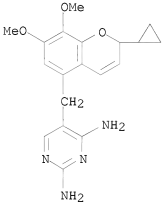
Absolute stereochemistry. Rotation (+).



IT 192315-05-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(enantioselective synthesis and photoracemization of cyclopropylchromenecarboxylate)
RN 192315-05-2 CAPLUS
CN 2H-1-Benzopyran-5-carboxylic acid, 2-cyclopropyl-7,8-dimethoxy-, methyl ester (CA INDEX NAME)



IT 192314-93-5P
RL: PNU (Preparation, unclassified); PREP (Preparation)
(enantioselective synthesis of cyclopropylchromenecarboxylate and formal synthesis of (aminopyrimidinylmethyl)cyclopropylchromene dihydrofolate reductase inhibitor)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



OSC.G 47 THERE ARE 47 CAPLUS RECORDS THAT CITE THIS RECORD (48 CITINGS)
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1997:479370 CAPLUS
DN 127:108943
OREF 127:21015a
TI Preparation of 5-(2,4-diaminopyrimidin-5-ylmethyl)-2H-1-benzopyranes as antibacterials
IN Masciadri, Raffaello
PA F. Hoffmann-La Roche Ag, Switz.
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9720839	A1	19970612	WO 1996-EP5151	19961122
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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	CA 2238521	C	20050816		
	AU 9676963	A	19970627	AU 1996-76963	19961122
	AU 708578	B2	19990805		
	EP 866791	A1	19980930	EP 1996-939890	19961122
	EP 866791	B1	20020130		
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	CN 1203600	A	19981230	CN 1996-198783	19961122
	CN 1092194	C	20021009		
	BR 9611871	A	19990217	BR 1996-11871	19961122
	JP 2000501399	T	20000208	JP 1997-520925	19961122
	JP 3309340	B2	20020729		
	EP 1149834	A1	20011031	EP 2001-117420	19961122
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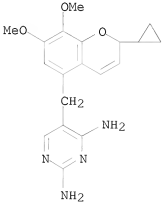
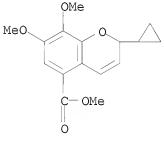
	AT 212629	T	20020215	AT 1996-939890	19961122
	PT 866791	E	20020531	PT 1996-939890	19961122
	ES 2169272	T3	20020701	ES 1996-939890	19961122
	US 5773446	A	19980630	US 1996-758993	19961202
PRAI	CH 1995-3425	A	19951204	cited in IDS	
	EP 1996-939890	A3	19961122		
	WO 1996-EP5151	W	19961122		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS MARPAT 127:108943
AB The title compds. [I; R1 = straight-chain C5-10-alkyl, branched C3-5-alkyl, C3-6-cycloalkyl, C3-5-ω-carboxyalkyl; R2, R3 = C1-5-alkyl; R1 = H; R2 = C3-5-ω-alkyl] and their pharmaceutically acceptable acid addition salts which have antibiotic properties and can be used in the control or prevention of infectious diseases, were prepared and formulated. Thus, treatment of guanidine.HCl with tert-BuOK in EtOH followed by addition of (RS)-3-anilino-2-(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-ylmethyl)acrylonitrile afforded I [R1 = cyclopropyl; R2, R3 = MeO]. Compound I [R1 = iPr; R2, R3 = MeO] showed IC50 of 0.001 μM against the purified DHFR of the reference strain S. aureus ATCC25923.
IT 192314-93-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 5-(2,4-diaminopyrimidin-5-ylmethyl)-2H-1-benzopyranes as antibacterials)
RN 192314-93-5 CAPLUS
CN 2,4-Pyrimidinediamine, 5-[(2-cyclopropyl-7,8-dimethoxy-2H-1-benzopyran-5-yl)methyl]- (CA INDEX NAME)



IT 192315-05-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 5-(2,4-diaminopyrimidin-5-ylmethyl)-2H-1-benzopyranes as antibacterials)
RN 192315-05-2 CAPLUS
CN 2H-1-Benzopyran-5-carboxylic acid, 2-cyclopropyl-7,8-dimethoxy-, methyl ester (CA INDEX NAME)



OSC.G 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                   274.57      466.82

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY     SESSION
CA SUBSCRIBER PRICE                                   -39.95      -39.95

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